DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

FY 2005 Budget — Page No.

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JUSTIFICATION
OFFICE OF AIDS RESEARCH

Budget Authority:

	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate	Increase or Decrease
Budget Authority	$2,716,218,000	$2,849,952,000	$2,930,397,000	$80,445,000

INTRODUCTION

The Global HIV/AIDS Pandemic

Group	People Newly Infected in 2003	People Living with HIV/AIDS in 2003	AIDS Deaths in 2003
Adults	4.2 Million	38.6 Million	2.5 Million
Women	*2.0 Million*	*19.2 Million*	*1.2 Million*
Children	700,000	2.5 Million	500,000
Total	5.0 Million	40.0 Million	3.0 Million

Source: UNAIDS

A new United Nations report, "The Impact of AIDS," presents a devastating picture of the global pandemic, highlighting its impact on families, agriculture and famine, business, healthcare, education, and national economic growth: "The HIV/AIDS epidemic has erased decades of progress in combating mortality and has seriously compromised the living conditions of current and future generations."[1] The United Nations General Assembly's Declaration of Commitment on HIV/AIDS states "...the global HIV/AIDS epidemic, through its devastating scale and impact, constitutes a global emergency and one of the most formidable challenges to human life and dignity, as well as to the effective enjoyment of human rights, which undermines social and economic development throughout the world and affects all levels of society – national, community, family, and individual."[2]

A CIA report stated, "By 2010, we estimate that five countries of strategic importance to the United States – Nigeria, Ethiopia, Russia, India, and China – collectively will have the largest number of

[1] "The Impact of AIDS" (Department of Economic and Social Affairs, United Nations, 2003).

[2] Ibid.

HIV/AIDS cases on earth."[3] *Foreign Affairs* magazine stated: "The spread of HIV/AIDS through Eurasia, in short, will assuredly qualify as a humanitarian tragedy – but it will be much more than that. The pandemic there stands to affect, and alter, the economic potential – and by extension, the military power – of the region's major states...Over the decades ahead, in other words, HIV/AIDS is set to be a factor in the very balance of power within Eurasia – and thus in the relationship between Eurasian states and the rest of the world."[4] Dramatic increases in HIV infection also are occurring in Eastern Europe, Central Asia, Latin America, and the Caribbean.

HIV has already infected more than 60 million people around the world, and AIDS has surpassed tuberculosis and malaria as the leading infectious cause of death worldwide.[5] Another dimension to the epidemic in Africa was cited in the *New York Times*: "As a result of HIV, the worst-hit African countries have undergone a social breakdown that is now reaching a new level: African societies' capacity to resist famine is fast eroding. Hunger and disease have begun reinforcing each other."[6]

HIV/AIDS GLOBAL CRISIS

- Reversing 3 decades of development gains
- National security issue
- Economic decline of 10-40%
- Health system chaos
- Political and military instability
- Famine
- Rapidly increasing number of orphans
- Immense humanitarian concerns

Curbing the transmission of HIV from infected mother to infant is an especially compelling challenge in resource-poor countries. The coexistence of other endemic diseases widely prevalent in developing countries, such as respiratory and gastrointestinal infections, complicate treatment and pose additional problems for medical personnel caring for HIV-infected individuals.

The Epidemic in the United States

The HIV/AIDS epidemic in the United States continues to evolve. According to CDC statistics, the decline in death rates observed in the late 1990s, due largely to expanded use of new antiretroviral therapies (ART) that prevent progression of HIV infection to AIDS, has now leveled off; and AIDS incidence increased 2 percent in 2002 (over 2001). This means that the overall epidemic is continuing to expand.[7] [8] [9] In addition, use of ART has now been associated with a series of side effects and long term complications that may have a negative impact on mortality rates. HIV infection rates are continuing to climb among women, racial and ethnic minorities, young

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[3] "Intelligence Community Assessment: The Next Wave of HIV/AIDS: Nigeria, Ethiopia, Russia, India, and China." (CIA, 2002).

[4] "The Future of AIDS," *Foreign Affairs*, November/December 2002.

[5] "Report on the Global HIV/AIDS Epidemic: July 2002," (UNAIDS/WHO, Geneva, Switzerland, 2002).

[6] A. de Waal, "What AIDS Means in a Famine," *New York Times*, 11/19/02.

[7] CDC Year-End HIV/AIDS Surveillance Report for 2002 (CDC, 2003).

[8] "Centers for Disease Control and Prevention HIV Prevention Strategic Plan Through 2005," (CDC, 2001).

[9] "HIV/AIDS Update – A Glance at the HIV Epidemic," (CDC, 2001).

homosexual men, individuals with addictive disorders, and people over 50 years of age.[7] [10] The appearance of multi-drug resistant strains of HIV presents an additional serious public health concern.[11] [12] [13] [14] [15] These data forebode an epidemic of even greater magnitude in the coming years.

According to CDC reports, approximately one quarter of the HIV-infected population in the United States also is infected with hepatitis C virus (HCV). HIV/HCV co-infection is found in 50 to 90 percent of injecting drug users (IDUs). HCV progresses more rapidly to liver damage in HIV-infected persons and may also impact the course and management of HIV infection, as HIV may change the natural history and treatment of HCV.[16]

AIDS disproportionately affects African Americans and Hispanics. According to CDC figures through December 2001, approximately 64 percent of newly infected women are African American and 17 percent are Hispanic. Among newly infected men, approximately 43 percent are African American and 20 percent are Hispanic.[17]

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[7] CDC Year-End HIV/AIDS Surveillance Report for 2002 (CDC, 2003).

[10] "U.S. HIV and AIDS Cases Reported through June 2000," *CDC HIV/AIDS Surveillance Report, Vol. 12* (2000).

[11] N. Loder, *Nature* 407, 120 (2000).

[12] H. Salomon et al., *AIDS* 14, 17 (2000).

[13] Y.K. Chow et al., *Nature* 361, 650 (1993).

[14] M. Waldholz, "Drug Resistant HIV Becomes More Widespread," *Wall Street Journal*, 2/5/99.

[15] "World Health Report on Infectious Diseases: Overcoming Antimicrobial Resistance," (WHO, Geneva, 2000).

[16] "Frequently Asked Questions and Answers About Coinfection with HIV and Hepatitis C Virus" (CDC, 2002).

[17] "U.S. HIV and AIDS Cases Reported through Dec. 2001," *CDC HIV/AIDS Surveillance Report, Vol. 13* (2001).

Setting the AIDS Research Priorities: Comprehensive Plan and Budget

To respond to this pandemic, the NIH has developed a comprehensive biomedical and behavioral research program to better understand the basic biology of HIV, develop effective therapies to treat and control HIV disease, and design interventions to prevent new infections from occurring. The Office of AIDS Research (OAR) develops an annual *NIH Plan for HIV-Related Research* that is based on the most compelling scientific priorities that will lead to better therapies and prevention strategies for HIV infection and AIDS. OAR has established an effective model for developing a consensus on the scientific priorities of the Plan, utilizing planning groups composed of NIH scientists and experts from academia and industry, as well as representatives from the AIDS community, who meet together to develop the Plan.

The Plan serves as the framework for developing the annual NIH AIDS budget; for determining the use of NIH AIDS-designated dollars; for tracking and monitoring expenditures; and for informing the scientific community, the public, and the AIDS-affected community about NIH AIDS research priorities. In collaboration with the Director of NIH, the OAR determines the total annual NIH AIDS research budget. Within that total, the OAR establishes the AIDS research budgets for each NIH Institute and Center, in accordance with the priorities and objectives of the plan. This budget request is framed on the scientific priorities and objectives of the *NIH FY 2005 Plan for HIV-Related Research*. The entire plan can be found on the OAR web site: http://www.nih.gov/od/oar/public/public.htm#PLAN.

The FY 2005 research agenda continues the following over-arching themes: research to prevent and reduce HIV transmission, including vaccines, microbicides, and behavioral interventions; research to develop therapies for those who are already infected; international research, particularly to address the pandemic in developing countries; and biomedical and behavioral research targeting the disproportionate impact of AIDS on minority populations in the United States. These efforts all require a strong foundation of basic science. The Plan establishes the NIH AIDS research agenda in the following Scientific Areas of Emphasis: Natural History and Epidemiology, Etiology and Pathogenesis, Therapeutics, Vaccines, and Behavioral and Social Science. The Plan also addresses the cross-cutting areas of: Racial and Ethnic Minorities; Women and Girls; Microbicides; HIV Prevention Research; International Research; Training, Infrastructure, and Capacity Building; and Information Dissemination. The key priorities for each research area and directions for future research are summarized below.

SCIENCE ADVANCES AND NEW INITIATIVES

THERAPEUTICS

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Advance the discovery and validation of new viral and cellular targets.
- Develop new therapeutic agents that: target drug-resistant virus; have activity in viral reservoirs and cellular compartments; and have improved pharmacologic and toxicologic properties.
- Determine optimal therapeutic strategies including when to start (early versus late), change, sequence, or interrupt therapies and evaluate therapeutic drug monitoring strategies.
- Identify regimens with improved toxicity, efficacy, pharmacokinetics, activity in viral reservoirs, adherence potential, and reduced cost.
- Target affected populations, especially women, injecting drug users (IDUs), children, adolescents, older adults, and across racial/ethnic groups. Conduct studies that permit evaluation of potential differences in response to therapy due to gender and/or racial/ethnic differences.
- Enhance capabilities for long-term followup and evaluate the long-term effects of therapy and the implications of these findings on public health.
- Conduct studies to evaluate the implications of therapy to prevent HIV transmission on public health.
- Develop safe, effective, feasible, and conveniently administered strategies to interrupt mother-to-child transmission (MTCT) of HIV. Focus on international studies to inhibit MTCT with special emphasis on breastfeeding.
- Conduct studies to evaluate and reduce short- and long-term toxicity of antiretroviral therapy (ART) to prevent HIV transmission in women during pregnancy, and in their offspring who were perinatally exposed.
- Evaluate the effects of co-infection, especially with hepatitis B virus (HBV), hepatitis C virus (HCV), tuberculosis (TB), or malaria, on the management of HIVdisease.
- Develop new agents for the treatment of HBV, HCV, TB, and malaria in the setting of HIV infection, with specific attention to pharmacologic drug interactions and nonoverlapping toxicity.
- Develop and evaluate therapeutic approaches including vaccines that will improve and sustain immune function or prevent transmission of HIV infection.
- Expand international clinical research programs in countries with limited resources.
- Design and conduct clinical studies that are appropriate for diverse international settings, including studies to improve and facilitate the delivery of therapeutic and prevention interventions for HIV disease.
- Evaluate the clinical and public health impact of prophylactic and therapeutic interventions for co-infections/opportunistic infections (OIs) endemic to international settings.
- Encourage studies that integrate therapeutic regimens and prevention interventions.

Today, many HIV-infected people are living with the benefits resulting from NIH-supported research in this area. The development of combination regimens including protease inhibitors has extended the length and quality of life for many HIV-infected individuals in the United States and Western Europe. Unfortunately, however, antiretroviral therapy (ART) has failed to eradicate HIV, and a growing proportion of patients receiving therapy experience treatment failure. Some patients find it difficult or impossible to comply with arduous treatment regimens, develop toxicities and side-effects, or cannot afford their high cost. Others fail to obtain a satisfactory reduction in viral load even while adhering to treatment regimens. An increasing number of treatment failures are linked to the increasing emergence of drug-resistant HIV. In addition, metabolic complications,

including insulin resistance, and body composition changes such as deforming deposits of abdominal adipose tissue, have emerged in individuals who have been on long-term antiretroviral regimens. These side-effects and complications appear to be increasing as HIV-infected patients continue on the drug regimens. More deaths occurring from liver failure, kidney disease, and cardiovascular complications are being observed in this patient population.

The need for simpler, less toxic, and cheaper drugs and drug regimens to treat HIV infection and its associated opportunistic infections (OIs), malignancies, and other complications, continues to be a critical priority. This includes the discovery and development of the next generations of antiviral drugs directed against new cellular and viral targets. Clinical trials will help to better define when to begin and/or switch drugs within a regimen, as well as to identify regimens for treatment-experienced individuals who no longer respond to these anti-HIV drugs. Antiretroviral and OI prophylaxis regimens are becoming increasingly complex with respect to drug-drug interactions and adherence. Protease inhibitors, in particular, interact with each other and many other medications commonly used by HIV-infected individuals. Additional research is under way and planned with the goal of minimizing viral replication and delaying disease progression, drug resistance, and development of manifestations such as metabolic complications and body composition changes. Important studies are planned to evaluate delayed and long-term effects of these antiretroviral drugs.

Studies are answering the following questions: When should ART be initiated? When should they be changed? How long can successful therapies maintain decreased viral loads, increased CD4 counts, and improved clinical outcomes? What is the basis for the emergence of drug resistance, and how can it be prevented? Can treatment strategies be developed for patients who no longer respond to current regimens? Can therapeutic approaches rebuild the immune system, so that disease progression is delayed? Can treatment strategies be developed to eliminate HIV, so that it is not transmitted from an infected individual to others?

Recent advances in therapeutics research underscore the importance of continued and further collaboration of Government- and industry-sponsored drug development research and clinical trials with the common goal of developing therapeutic regimens that slow disease progression, extend life spans, and improve the quality of life for HIV-infected individuals.

THERAPEUTICS RESEARCH ACCOMPLISHMENTS

- Extended and improved quality of life for many HIV-infected individuals
- Reduced AIDS deaths
- Decreased morbidity due to opportunistic infections
- Reduced pediatric mortality
- Demonstration that combinations of antiretroviral agents can significantly reduce viral load in many patients to undetectable levels and increase CD4 counts
- Revolution in design and testing of drugs and diagnostic methodologies benefits other diseases
- Findings contributed to approval of AIDS-related therapies by FDA and development of guidelines for their optimal use

ETIOLOGY AND PATHOGENESIS

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Facilitate the translation of new insights into HIV biology to develop novel interventions for the prevention and treatment of HIV infection. Identify and validate cofactors for viral genes as new targets capitalizing on novel technologies including viral interference and genomic screening.
- Elucidate the biologic determinants of HIV transmission between individuals, and define the mechanisms by which host factors, viral factors, and cofactors may influence the process of virus transmission and dissemination.
- Understand the dynamics of virus-host interaction through the course of HIV infection.
- Investigate the mechanisms of persistence of HIV infection.
- Develop innovative technologies in human and nonhuman primate immunology to guide vaccine development and immune reconstitution efforts.
- Advance the understanding of the mechanisms responsible for the toxicities and long-term complications of antiretroviral therapy (ART) and the factors that underlie changes in the causes of morbidity and mortality in an era of increasingly effective therapies.

Of paramount importance in our fight against HIV/AIDS is maintaining a strong commitment to basic research. Tremendous progress has been made in understanding the fundamental steps in the life-cycle of HIV, the host-virus relationship, and the clinical manifestations associated with HIV infection and AIDS. Groundbreaking research on basic HIV biology and AIDS pathogenesis has revolutionized the design of drugs, the methodologies for diagnosis, and the monitoring for efficacy of antiviral therapies. In spite of these achievements, we still do not have a clear understanding of major aspects of viral interaction with the infected individual, the nature of the immune response to the virus, how the virus establishes infection and spreads throughout the body, and its mechanisms of pathogenesis. This basic knowledge is critical for our efforts to prevent and control HIV infection and disease progression. A substantial portion of NIH AIDS-related research will continue to be devoted to basic research.

ETIOLOGY AND PATHOGENESIS ADVANCES

- Identification of key HIV components as drug targets
- Identification of macromolecular structure of viral components for drug design
- Identification of chemokines as co-receptors
- Identification of viral reservoirs as sites of latent infection

Some of the outstanding questions within the area of etiology and pathogenesis research include: What role do the specific products of HIV (the viral genes and their protein products) play in the viral life cycle in individual cells and within the body of infected individuals? How is HIV transmitted between cells and between individuals? What contribution does the immune system make to controlling the infection and to the disease process? What mechanisms are involved in cell injury and death in the immune, nervous, and other systems that HIV affects? What host factors and cofactors influence the course and outcome of HIV infection? What is the relationship of HIV infection to the associated malignancies, opportunistic infections (OIs), neurological impairments, and metabolic abnormalities that characterize AIDS?

Research is focusing on the different mechanisms of viral persistence to understand the reasons for drug failure, to design rational approaches for virus eradication, and to better assess the impact of persistence on HIV transmission and its implications for HIV prevention. HIV can persist in a latent reservoir of resting memory CD4 T cells that is established very early after infection and by continuously replicating, albeit at very low levels, even in the presence of antiretroviral therapies that can drive viral load below the limits of detection.

Understanding the normal development and functioning of the human immune system is crucial to our ability to understand the effects of HIV on the immune system and the pathogenesis of AIDS. This understanding also holds the key to designing rational immune reconstitution approaches in persons undergoing antiretroviral treatment and identifying the characteristics of the immune response that are needed for a protective vaccine.

The basic science underlying HIV etiology and pathogenesis research is generally gender neutral. Basic mechanisms of viral replication and pathogenesis are not expected to differ in women and men. However, there are differences in the way HIV infection is transmitted and how the disease is manifested in women and men. Studies have been designed to elucidate the pathogenic mechanisms more commonly observed in women, children, and adolescents infected with HIV. Transmission of HIV from a mother to her infant may occur *in utero* through transplacental passage of virus, during delivery, or after birth through breast-feeding. Many basic research questions associated with maternal-fetal transmission remain unclear and are actively under investigation.

AIDS is associated with a broad spectrum of cancers and tumors. As HIV causes immunosuppression and most AIDS-associated malignancies are strongly associated with viruses, HIV infection provides a unique model to study the interplay of viruses, a dysfunctional immune system, and the development of cancers. Elucidation of the interactive factors involved in the pathogenesis of AIDS-associated malignancies will possibly translate into the identification of new targets for prevention and treatment.

HIV infection results in the progressive damage of the immune systems of infected individuals and makes them susceptible to a diverse collection of bacteria, viruses, fungi, and protozoa that represent the major causes of suffering and death for HIV-infected individuals. Opportunistic infections can affect virtually every tissue and organ system in the body, resulting in severe functional compromise. NIH currently supports a comprehensive portfolio of basic research on the pathogenesis of AIDS-associated OIs.

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Sponsor domestic and international epidemiologic studies to characterize modes of transmission, including host characteristics (e.g., sexual behavior, substance use, use of blood products and other injections, genetic variations) and viral characteristics, or continued risk behaviors in HIV-infected and uninfected populations of adults, adolescents, and children.
- Implement epidemiologic studies (including those of host genetics and other modifiers of host response, viral genetics, and transmission characteristics) to monitor, inform, and evaluate intervention strategies and surveillance in domestic and international settings.
- Develop and evaluate accurate, reproducible, and affordable virologic, immunologic, pharmacologic, and genetic assays; measures of adherence to therapy; and markers of recent infection for high-throughput use in domestic and international settings.
- Develop, maintain, and effectively utilize domestic and international cohorts, repositories, and nested studies among populations experiencing emerging and ongoing HIV epidemics to establish databases that support analyses of host and viral characteristics. Use this approach to increase the understanding of the pathogenesis of HIV infection and disease, including adverse events in the presence of interventions.
- Characterize the interactions between HIV, host genetics, and the major environmental factors that influence outcomes (viral transmission, response to therapy, and disease progression). This includes how variants of viral genes (e.g., those accounting for subtypes and drug resistance) interact with the host in the context of different routes of transmission, co-morbidities, and host genetic variants or other determinants of the immune response.

Natural history and epidemiologic research is needed to monitor epidemic trends, develop and evaluate prevention modalities, follow the changing clinical manifestations of HIV disease in different populations, and measure the effects of treatment regimens. NIH will continue to support research to examine topics in HIV transmission, HIV/AIDS disease progression (including the occurrence of opportunistic infections), malignancies, metabolic complications, neurological and behavioral dysfunctions, and the development of other HIV/AIDS-related conditions. Domestically, as well as internationally, the populations affected by HIV/AIDS are also those most severely affected by the spreading epidemics of sexually transmitted diseases (STDs), TB, and other co-morbidities, such as Hepatitis C. Researchers are studying the effects of viral, host, and other factors on transmission and disease progression. Since biological, pharmacological, psychological, and behavioral factors all potentially influence the impact of antiretroviral therapies on HIV transmission, researchers are evaluating the specific contributions of these factors and their net impact on HIV transmission. Research also is focusing on determining the biological characteristics, sociocultural factors, and health services issues that contribute to the differential dynamics of HIV transmission and disease progression in men, women, and in different racial/ethnic groups. Results from these studies

NATURAL HISTORY AND EPIDEMIOLOGY RESEARCH ACCOMPLISHMENTS

- CD4 and viral load established as biomarkers for disease progression and response to therapy
- Gender differences: women seroconvert at lower viral load than men
- Regimens to prevent opportunistic infections initiated at 200 CD4 level or less
- Presence of Hepatitis G virus (GBV-C) predicts survival

will provide new directions and improvements in HIV/AIDS prevention and care. NIH will continue to emphasize the importance of epidemiologic studies to investigate the mechanisms of disease progression, the causes of death, and the impact of therapy in changing the spectrum of HIV disease. The expansion of existing study populations in the United States will allow the identification of long-term effects of HIV therapy. The assembly of new, representative cohorts, specimen repositories, and databases in developing countries will be important to study key co-factors that modify HIV disease. NIH will foster basic and applied research to develop inexpensive virologic, immunologic, and genetic assays for use in domestic and developing country settings.

BEHAVIORAL AND SOCIAL SCIENCE

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Better understand and address through interventions the interactions among psychological, social, economic, and cultural dynamics of gender and sexuality that play a role in promoting sexual health or conferring sexual risk related to HIV transmission.
- Understand and address the disparate risks and consequences of HIV infection, as well as access, utilization, and quality of prevention and health care services among individuals and groups differing by socioeconomic status, geographic location, gender, sexual orientation, age, and ethnicity.
- Identify and address issues related to the sustainability and renewal of HIV/AIDS risk-reduction efforts at the individual, dyadic, group, and community levels over time, including changing perceptions and risk behaviors associated with the development of new HIV treatments, services, and prevention technologies.
- Conduct and support translational, operations, and health services research to understand better and address through interventions the barriers to and facilitators of the implementation of science-based HIV/AIDS interventions at the local community level.
- Support research on the interactions between individual and environmental (including social, structural, and cultural) factors and contexts that contribute to the co-occurrence of HIV/AIDS, other infectious diseases (e.g., tuberculosis [TB], sexually transmitted diseases [STDs], and hepatitis), substance use, mental illness, and homelessness; and support intervention research to address such co-occurring conditions.

NIH supports research to further our understanding of how to change the behaviors that lead to HIV transmission—including preventing their initiation—and how to maintain protective behaviors once they are adopted in all populations at risk. NIH sponsors research related to: developing, implementing, and evaluating behavioral and social interventions to reduce HIV transmission in a range of populations and settings; strengthening our understanding of the determinants, trends, and processes of HIV-related risk behaviors and the consequences of HIV infection; developing and evaluating behavioral strategies for preventing or ameliorating the negative physical, psychological, and social consequences of HIV infection; and improving the research methodologies employed in behavioral and social science research. A better understanding of social and cultural factors associated with HIV risk or protection, particularly in minority communities, will contribute to the successful implementation of a broader range of preventive or therapeutic measures. Drug users and their sex partners are the fastest growing segment of AIDS cases in the U.S. and in many other countries. Priority is being given to research that bridges and builds upon studies of the

phenomenon of addiction itself, the complex interaction of alcohol use, drug use, and poor impulse control, and to developing effective HIV-related interventions from that knowledge base.

BEHAVIORAL AND SOCIAL SCIENCE RESEARCH ADVANCES

In study populations, research on interventions to reduce risk demonstrated:

- Delayed sexual debut
- Reduced number of sex partners
- Increased protective behaviors
- Increased referral to drug and alcohol addiction treatment
- Development of supportive policies and programs

The development of new and more effective anti-HIV drugs and drug combinations has raised a host of behavioral issues. Lack of complete adherence to drug regimens may result in the development of drug-resistant strains of HIV, which could have devastating public health implications. In addition, HIV-infected individuals taking antiretroviral therapies who experience improved health and a decline in detectable virus may believe that they are less infectious and may lapse into unsafe sexual and drug-using behaviors. This could have the effect of increasing HIV transmission, if the virus is still viable at undetectable levels. These issues highlight the importance of research on how best to ensure adherence to both pharmacological and behavioral HIV-related interventions.

VACCINES

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Accelerate vaccine candidates from concept to clinical trials: identify ways to centralize or partially centralize and/or streamline efforts and to develop a systematic approach to make and qualify products, produced under good laboratory practice (GLP) and good manufacturing practice (GMP), for testing in both preclinical and initial clinical studies.
- Conduct comparative studies in preclinical evaluation of HIV vaccine candidates. Develop standardized, validated assays with reagents of known identity and source. A panel of immunological assays should include expanded assessment of cellular immunity and neutralizing antibodies, reagents to test specific responses, and easy access for both academic and industrial investigators to a standard panel of viral isolates for testing intersubtype and intrasubtype viruses.
- Continue to support basic research to feed new products into the vaccine pipeline.
- Design and conduct clinical trials with special attention to the issues of immunologic sub-types, genetic variants, and their importance to vaccine design. Incorporate the testing of vaccines representing different immunotypes in populations where intersubtype and multiple genetic subtypes are present.
- Continue and expand the initial efforts to educate high-risk populations and communities about HIV vaccines. In particular, continue to develop tools, devise outreach programs, and implement strategies to involve adolescent populations in HIV vaccine trials that will be testing products for efficacy.
- Continue to support the development of breeding colonies, appropriate biosafety housing, and most effective use of specific pathogen-free (SPF) non-human primates for HIV vaccine research and immunogenicity studies.
- Accelerate testing of vaccines and monoclonal antibody interventions in infants born to HIV-infected mothers in situations where breastfeeding cannot be avoided.
- Address new challenges in testing, and diagnosis of HIV infection in vaccinated individuals.
- Provide training of staff at clinical trial sites.

Safe and efficacious vaccines to prevent HIV infection and disease and/or transmission are essential for global control of the AIDS pandemic. As a result of increased funding from NIH in the area of HIV vaccines, many new approaches to HIV vaccines are being pursued. Basic research in vaccine design and studies of immune responses in small animals and non-human primates (NHP) as well as vaccine product development are underway. Recent HIV vaccine research studies in animal models have provided strong scientific rationales to further explore and develop several vaccine concepts and to move additional candidate vaccines into clinical testing. Although production of candidate vaccines for clinical study has proceeded slowly, at least 10 new candidate vaccines will enter Phase I trials in the next 2 years. Several new combinations of products, which are expected to provide better immune responses, also will be tested in Phase I or II trials. The Dale and Betty Bumpers Vaccine Research Center recently launched the first Phase I clinical trial of a multi-clade, multi-gene vaccine candidate.

VACCINE RESEARCH ACCOMPLISHMENTS

- More than 30 products or combinations tested in over 50 phase I and II trials with more than 4,000 volunteers
- New vaccine designs developed; 10-12 to enter phase I clinical trials within 2 years
- First multigene, multiclade Phase I trial launched by NIH Vaccine Research Center

NIH continues to increase support for a broad program encompassing basic, preclinical, and clinical research on candidate vaccine products. As promising candidates move further in the vaccine pipeline, expanded trials with populations at increased risk for HIV infection will become increasingly important. HIV/AIDS vaccine research requires trained health care, medical research, and prevention specialists, as well as populations at risk who will be integrally involved in the development of vaccine candidates and clinical vaccine and prevention trials. International and domestic sites are being developed, including a cadre of trained personnel, to conduct vaccine trials.

One of the foremost priorities for testing candidate vaccines continues to be a resolution of the crisis in the supply of monkeys available for HIV/AIDS vaccine studies. The supply of NHP, particularly rhesus macaques, for AIDS research and other areas of biomedical research remains a major problem for NIH-funded investigators. Both the supply of animals and the available space for conducting experiments that require adequately controlled biosafety housing are limiting and impeding exploration of new concepts in HIV vaccines. NIH is working to find solutions to these obstacles.

The development of an HIV vaccine is a complex research challenge because HIV is unusually well-equipped to elude immune defenses, as exemplified by its ability to vary extensively, to persist in viral reservoirs, and to eventually overcome the immune system. Many different vaccine approaches are being pursued. Initial studies are leading to more advanced vaccine candidates that may provide better protection. NIH has now conducted more than 50 Phase I and two Phase II clinical trials of more than 30 vaccine candidates, individually or in combination, in human volunteers in collaboration with academic investigators and industry co-sponsorship.

MICROBICIDES

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Promote innovative mechanisms of funding to attract additional investigators to undertake multidisciplinary research on microbicides discovery and development.
- Foster the development of varieties of microbicidal products that are based on specific biological and physiological pathways involving mucosal routes of HIV transmission.
- Identify relevant practical and accessible methodologies to assess preclinical/clinical safety and activity of microbicides in a standardized fashion.
- Foster the development of combination approaches in acceptable formulations, such as chemical and physical barriers, and microbicides with different specificities and mechanisms of action to prevent transmission and acquisition of HIV and other sexually transmitted infections.
- Promote innovative methods to develop and assess acceptable formulations and modes of delivery for microbicides, bridging knowledge and applications from multiple scientific disciplines.
- Expand capacity (infrastructure and human resources) and strengthen coordination to conduct Phase II/III microbicides clinical trials.
- Conduct social and behavioral research in concert with microbicides clinical trials, including research on product use, sexual behaviors, and the identification of reliable and valid behavioral measures for use in trials.

The vulnerability of women to acquiring HIV infection requires the development of effective and acceptable female-controlled chemical and physical barrier methods, such as topical microbicides, to reduce HIV transmission. NIH supports a comprehensive research program that includes the screening, discovery, development, preclinical *in vitro* and *in vivo* testing, and clinical evaluation of compounds with the potential to act as antimicrobial agents with both spermicidal and nonspermicidal activity. NIH closely collaborates with academia and industry to identify and explore new and existing compounds as potential topical microbicidal agents.

Animal model testing and toxicity studies of potential candidate compounds are conducted through NIH-sponsored contracts before these agents are considered for clinical trials. NIH also supports Phase I, II, and III clinical trials of various topical microbicides, as well as behavioral and social research on the acceptability and use of microbicides among different populations. Important areas of research include the establishment of clinical trial sites and the necessary infrastructure to conduct those trials, especially in developing countries; the development of criteria for selecting potential products to be evaluated in clinical trials and for advancing them through the different phases of clinical studies; and research on ethical and behavioral issues impacting clinical trials.

PREVENTION RESEARCH

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Examine the ways in which social, economic, cultural, and environmental conditions, including stigma and discrimination, contribute to, or create sources of, HIV-related risk; and develop interventions based on this understanding.
- Elucidate the prevention-treatment interface, including the effects of HIV/AIDS treatment availability, delivery, success, and failure on HIV transmission and acquisition, and the integration of prevention into clinical care.
- Further explore, develop, and evaluate alternative methods to the randomized controlled trial (RCT) for testing the efficacy of multidisciplinary HIV preventive interventions when RCTs are inappropriate or impossible to conduct; and develop guidelines to inform the field about when such non-RCT methods are appropriate to employ.
- In collaboration with other governmental and nongovernmental organizations, enhance support for operations, health services, and evaluation research on the design, adaptation, testing, and implementation of evidence-based HIV prevention strategies; and assess the impact of such strategies on risk behaviors at the population level.

NIH supports a comprehensive prevention science research agenda that targets interventions to both infected and uninfected at-risk individuals to reduce HIV transmission. Biomedical prevention research priorities include the development of topical microbicides, strategies to prevent mother-to-child transmission (including a better understanding of HIV risk associated with breast-feeding), and management of sexually transmitted diseases (STDs). NIH behavioral research strategies include interventions related to drug and alcohol use and risky sexual behaviors. Research efforts continue to identify the most appropriate intervention strategies for different populations and sub-epidemics in the United States and around the world.

PREVENTION RESEARCH AGENDA

- Vaccines
- Topical microbicides
- Behavioral research
- Reducing transmission due to substance abuse
- STD control
- Antiretroviral therapy as prevention

These HIV prevention research activities include both basic and intervention studies. Research that elucidates the fundamental mechanisms of human behavior and disease transmission and progression provides the essential basic knowledge needed for the development of testable interventions. Studies examine the range and interaction of biological, neurological, psychological, familial, social network, and other environmental factors that have an impact on HIV transmission, acquisition, or protection. While the focus of the NIH HIV prevention research program is on primary prevention of new HIV infections, it also addresses secondary prevention, that is, prevention of the negative physiological, psychological, and social consequences of disease among individuals already infected with HIV and their families, networks, and communities. This includes identifying potential co-factors, correlates, and mediators of disease progression, and developing biomedical and/or psychosocial interventions to address them.

RACIAL AND ETHNIC MINORITIES

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Expand prevention research in racial and ethnic minority communities to identify effective and innovative strategies to reduce HIV transmission.
- Promote and expand capacity building and infrastructure development for HIV/AIDS research in racial and ethnic minority communities. An emphasis on community-academic-government partnerships, with concurrent development of minority institutions and investigators, is necessary for these communities to develop and sustain effective efforts to control HIV infection and its consequences.
- Develop, test, and evaluate novel survey instruments and methodologies for racial and ethnic minority communities that are culturally and contextually appropriate.
- Develop, implement, and evaluate an HIV/AIDS research agenda that links the science of HIV/AIDS to the challenges that confront these communities, translating the findings into utilizable practical strategies.
- Expand methods for the rapid dissemination of scientific findings to minority communities. This is an essential component of developing community involvement and nurturing community infrastructure development necessary to control the ongoing epidemic.

HIV infection, like many other disease states, reflects the ongoing health disparity among racial and ethnic minority communities. Prevalence of HIV infection in racial and ethnic minority communities is disproportionately higher than in majority communities. In many U.S. urban centers, the prevalence of HIV infection mimics rates found in the developing world. These findings, along with the resurgence of STDs and associated high-risk behaviors, demonstrate the need for comprehensive strategies to decrease HIV transmission in affected vulnerable populations, and improve treatment options and treatment outcomes.

MINORITY INITIATIVES

- Minority-targeted research, primarily prevention
- Initiatives to increase minority enrollment in clinical studies
- Minority training, infrastructure, and research capacity-building initiatives
- Grantsmanship workshops for minority researchers
- Regional Technology Transfer Program
- Community outreach programs

OAR is directing increased resources toward research to develop new interventions that will have the greatest impact on these groups. These include interventions that address the co-occurrence of other STDs, hepatitis, drug abuse, and mental illness; and interventions that consider the role of culture, family, and other social factors in the transmission and prevention of these disorders in minority communities. NIH is making significant investments to improve research infrastructure and training opportunities for minorities and will continue to assure the participation of minorities in AIDS clinical trials, as well as in natural history, epidemiologic, and prevention studies. OAR has provided additional funds to projects aimed at increasing the number of minority investigators conducting behavioral and clinical research; targeting the links between substance abuse, sexual behaviors, and HIV infection; increasing outreach education programs targeting minority physicians and at-risk populations; and expanding the portfolio of population-based research. One of these projects is a series of Training and Career Development Workshops for racial and ethnic minority

investigators. These workshops provide minority investigators with an opportunity to learn more about available NIH funding mechanisms and to meet and network with senior minority investigators who receive significant levels of NIH funding.

NIH supports a broad array of behavioral intervention studies with specific focus on African American populations. These studies are characterizing the disease process in drug users, factors influencing disease progression, consequences of multiple co-infections, effectiveness of therapeutic regimens, and the impact of health care access and adherence to therapeutic regimens on disease outcomes. The increasing number of minority AIDS cases underscores the importance of research to define and utilize cultural, social, and contextual factors that affect HIV risk behaviors. The role of alcohol and drug use in facilitating HIV transmission through social networks in all communities also is being explored within these social frameworks.

WOMEN AND GIRLS

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Study the biology of the reproductive tract of HIV-infected and HIV-uninfected women and girls, integrating studies of physiology, immunology, microbiology, and anatomy.
- Elucidate a range of host-virus interactions through the course of HIV infection (in particular, during primary HIV infection) and across the life cycle in women and girls.
- Develop and continue clinical studies—including biological, therapeutic, vaccine, natural history, epidemiological, behavioral, and social—to ascertain the effects of sex and gender in HIV infection among women and girls; and ensure dissemination of resulting information.
- Enhance basic behavioral and social research (theoretical and methodological) on gender construction, maintenance, dynamics, and consequences—including gender-based stigma and discrimination; and integrate this work into the design and evaluation of HIV prevention and care interventions.
- Explore factors that influence development, adoption, use, and effectiveness of women-controlled methods (including physical and chemical barrier methods), alone or in combination, for preventing HIV transmission and acquisition; and ensure dissemination of resulting information.
- Enhance opportunities and mechanisms for recruiting and training biomedical, behavioral, and social scientists in the conduct of interdisciplinary sex and gender analyses in HIV/AIDS research.

Women experience HIV/AIDS differently from men both physiologically and socially. NIH research has demonstrated that women progress to AIDS at lower viral load levels and higher CD4 counts than do men. This finding may have implications for care and treatment of HIV-infected women, particularly with antiretroviral therapy. Women's childbearing capacity also differentiates their HIV/AIDS experiences from men's, as HIV-infected pregnant women may transmit the virus to their fetuses and infants. Women in most societies are the primary care providers for children and older people, so their early deaths from AIDS and its complications often leave dependents with no one to care for them. NIH researchers are studying the ways in which sex and gender confer vulnerability to, or protection from, HIV infection and AIDS among women and girls—in general, and relative to men—in diverse geographical settings and during different stages of the life course. There are many research questions that remain unanswered about specific anatomical and physiological characteristics of women and girls that might play a role in transmission, acquisition,

or resistance to HIV infection. Studies will focus on factors in HIV acquisition, including the influence of hormonal modulation on viral replication and immune responses in the reproductive tract, and co-factors, such as coincident infections with other STD pathogens.

INTERNATIONAL AIDS RESEARCH

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Develop in-country research and training infrastructure for the conduct of effective prevention and treatment interventions research, integrating new activities into existing health care and prevention services where possible.
- Define the spectrum of HIV-related illnesses in diverse geographic settings and develop effective prevention and treatment interventions to limit their impact, with special emphasis on tuberculosis.
- Study the appropriate introduction and long-term use of antiretroviral therapy in resource-diverse settings.
- Support studies to develop prevention interventions appropriate to particular settings, with a particular focus on addressing prevention of HIV transmission from mother to child and drug and alcohol use and their associated risks in transmitting and acquiring HIV infection.
- Address challenges and barriers that impede the conduct of international research.

The UNAIDS report, *AIDS Epidemic Update: December 2001*, states that "AIDS has become the most devastating disease humankind has ever faced." HIV/AIDS is the fourth largest killer worldwide; in sub-Saharan Africa, it is the leading cause of death. The impact of AIDS on the developing nations of Africa, Asia, Europe, and Latin America is staggering, with even greater potential disaster to come. The cost in lost productivity and profitability, sickness and death, and a significant reduction in the skilled workforce in developing countries will have major economic impact for the United States and the world economy and security.

NEW CHALLENGE: CLINICAL EVALUATION OF THERAPIES IN INTERNATIONAL SETTINGS

- Expand therapeutic studies into international sites
- Develop research capacity and infrastructure
- Design studies to improve and facilitate delivery of therapeutic interventions
- Evaluate clinical and public health impact of antiretroviral treatment
- Integrate therapeutic regimens and prevention interventions

Since the early days of the epidemic, NIH has supported research efforts in countries affected by HIV and AIDS. Beginning in 1984 with a research project in Haiti and the establishment of Projet SIDA in 1985 in what was then Zaire, NIH has maintained a strong international research portfolio. NIH has expanded its research effort to encompass approximately 85 countries around the world. Results of this research benefit not only the people in countries where the research is conducted, but people affected by HIV/AIDS worldwide. NIH international research includes efforts to develop: HIV vaccine candidates and chemical and physical barrier methods, such as microbicides, to prevent sexual transmission; behavioral strategies targeted to the individual, family, and community to alter risk behaviors associated with sexual activity and drug and alcohol use; drug and non-drug strategies to prevent mother-to-child

transmission (MTCT); therapeutics for HIV-related co-infections and other conditions; and approaches to using ART in resource-poor settings.

Before prevention and treatment interventions can be implemented in different geographic settings, their safety must be confirmed and efficacy demonstrated in such settings through clinical trials and other intervention research. To develop vaccines and other prevention strategies that will be effective globally, phase I safety studies are first conducted in small populations in the U.S. To establish efficacy, large numbers of at-risk study participants are necessary. Around the world, the predominant mode of HIV transmission is heterosexual. Among heterosexuals in the United States, the rate of HIV infection is estimated to be approximately 1.5%. In some developing counties, the rate of heterosexual HIV infection is 13-25%. Because of the large populations at high-risk of infection, prevention studies can be more efficiently conducted in those settings.

Although industrialized nations have experienced a dramatic decrease in transmission of HIV from infected mother to her child, preventing this transmission is a significant challenge in resource-poor settings of the world; strategies that can effectively be used in such settings continue to be pursued. Research also is needed to devise strategies to decrease transmission in medical settings.

Development of a research infrastructure is essential to these research programs. Specific international infrastructure needs include: (1) developing research sites through establishment of stable, targeted cohorts, development of recruitment strategies, and enhancement of laboratory, clinical, and data management capabilities; (2) increasing the number of scientists, clinicians, and health care workers trained in basic, clinical, and behavioral research, data management, and ethical considerations; (3) developing research collaborations; and (4) transferring appropriate clinical and laboratory technologies.

TRAINING, INFRASTRUCTURE, AND INFORMATION DISSEMINATION

RESEARCH PRIORITIES OF THE FY 2005 PLAN

- Continue to support training of domestic and international biomedical and behavioral AIDS researchers, including programs designed to recruit individuals from minority communities into research careers and to build research infrastructure in minority institutions.
- Continue to support improvement of facilities and equipment for the conduct of domestic and international AIDS research, including support of animal facilities for animal model research.
- Continue to support effective information dissemination approaches among researchers, health care providers, and affected communities to rapidly translate research findings into practice.

The NIH will continue to support training of domestic and international biomedical and behavioral AIDS researchers, as well as the improvement of facilities and equipment for the conduct of AIDS-related research, including facilities for animal model research. Numerous NIH-funded programs have increased the number of training positions for AIDS-related research, including programs specifically designed to recruit individuals from minority communities into research careers and to build research infrastructure in minority institutions. The NIH Loan Repayment Program (LRP)

was mandated by Congress under Public Law 100-607 in 1988 and authorized under 42 USC 288-1 to encourage health professionals to engage in AIDS-related research at the NIH. NIH also sponsors programs to train scientists in developing countries to undertake AIDS research. The National Primate Research Centers (NPRC) Program, provides specialized facilities, scientific and technical personnel, animal models research and breeding, and a wide variety of non-human primate species to support diverse requirements for AIDS-related research.

Effective information dissemination approaches will continue to be integral to HIV prevention and treatment efforts. Such programs are critical in light of the continuing advent of new and complex antiretroviral treatment regimens, the adherence issues related to HIV/AIDS treatment, the need for research communities to work and communicate globally, and the need to translate behavioral and social prevention approaches into practice. The changing pandemic and the increasing number of HIV infections in specific population groups, such as minorities and women, also underscore the need to disseminate HIV research findings and other related information to communities at risk. The flow of information among researchers, health care providers, and the affected communities represents new opportunities to rapidly translate research results into practice and to shape future research directions.

MANY OTHER DISEASES BENEFIT FROM AIDS RESEARCH

AIDS research is unraveling the mysteries surrounding many other infectious, malignant, neurologic, autoimmune, and metabolic diseases. AIDS research has provided an entirely new paradigm for drug design, development, and clinical trials to treat viral infections. For example, the drug known as 3TC, developed to treat HIV/AIDS, is now the most effective therapy for chronic hepatitis B infection. Drugs developed to prevent and treat AIDS-associated opportunistic infections also provide benefit to patients undergoing cancer chemotherapy or receiving anti-transplant rejection therapy. AIDS research also is providing a new understanding of the relationship between viruses and cancer.

AIDS RESEARCH BENEFITS OTHER DISEASES

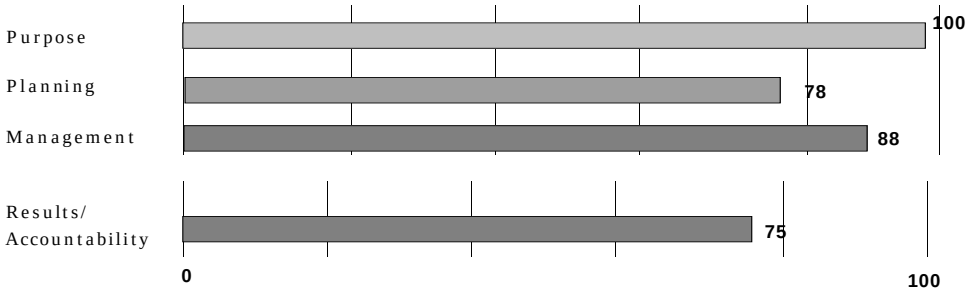
- New paradigm for viral research and drug design
- Established concept of "prophylaxis" of opportunistic infections in immuno-suppressed persons
- Provides unique model to study the role of the immune system in the emergence of cancers, and to test novel approaches by which immune responses can be modified to help treat malignancies (KS, NHL, cervical cancer)
- New approaches for rapid and sensitive diagnosis of disease and monitoring of treatment is applicable to other infectious diseases.
- Understanding of HIV-associated wasting of benefit to persons with cancer and other diseases
- 3TC and other drugs and drug combinations developed for HIV now standard of care for Hepatitis B and C
- Drugs for opportunistic infections used for transplant or immuno-suppressed patients
- Design of clinical trials, including community involvement

PROGRAM ASSESSMENT RATING TOOL (PART): ASSESSMENT OF NIH AIDS PROGRAM

The NIH AIDS program received an overall score of 83 in the OMB's 2005 Program Assessment Rating Tool (PART). This score included a 100 percent in the Program Purpose and Design section. The human and economic toll of the AIDS pandemic requires a unique response that is complex, comprehensive, multi-disciplinary, and global. The NIH role in this response is unprecedented, comprising a comprehensive program of basic, clinical, and behavioral research on HIV disease to better understand the basic biology of HIV, develop effective therapies and prevention strategies. The PART demonstrated that NIH provides effective scientific coordination and management of this diverse AIDS research portfolio through a comprehensive planning and budget development process, which was utilized to develop the FY 2005 budget request. NIH is enhancing collaboration, minimizing duplication, and ensuring that precious research dollars are invested in the highest priority areas of scientific opportunity that will allow NIH to meet its scientific goals.

Program: HIV/AIDS Research

Agency: Department of Health and Human Services
Bureau: National Institutes of Health



Key Performance Measures	Year	Target	Actual
Long-term Measure: By 2010, develop an HIV/AIDS vaccine. 2005 Targets: 1) Expand breeding of non-human primates: 3 centers; 2) Test 1 new virus stock; 3) Test 2 vaccine candidates in animals; 4) Phase I human trials: 1 vaccine candidate; 5) Seroincidence data: 3 sites; 6) Evaluate vaccine safety: 2 labs; 7) Initiate 4 phase I and II vaccine trials; 8) Produce candidate vaccine for phase III trials.	2005	See targets	
	2007	original date	
	2010	revised date	
Long-term Measure: By 2007, evaluate the efficacy of 3 new treatment strategies for HIV infection in phase II/III clinical trials.2005 Targets: 1) Develop 3 anti-HIV compounds; 2) Initiate 4 drug clinical trials; 3) Develop/test 2 agents to prevent/treat drug complications; and 4) Develop/test 1 new approach to inhibit mother-to-child transmission.	2005	See targets	
	2007	3 new treatment	

Rating: *Moderately Effective*

Program Type: *Research & Development*

Program Summary:

The National Institutes of Health (NIH) HIV/AIDS research grants were first awarded in 1983 in direct response to an emerging public health threat. The Office of AIDS Research was established in 1988 and given increased authority in 1993 to plan and coordinate NIH AIDS activities. Nearly 60 million people worldwide cumulatively have been infected with HIV, and the disease has killed more than 20 million people. The program's overarching priorities are: 1) prevention research to reduce HIV transmission (vaccine and microbicide development and behavioral interventions); 2) therapeutic research to develop simpler, less toxic, and cheaper drugs to treat HIV infection and complications; 3) international research; and 4) minority AIDS research.

The assessment found that the program has demonstrated some progress and is moderately effective overall. Additional findings include:

- The program has a flexible and cross-cutting program design that explicitly gives the NIH Office of AIDS Research the responsibility to plan, coordinate, fund, and evaluate AIDS research priorities across NIH Institutes.
- The program has a limited number of specific long-term performance measures that focus on outcomes.
- The program develops an annual comprehensive strategic plan, which is used to both develop the budget and to track expenditures; however, budget and performance are not explicitly aligned.
- Audited financial statements cited delays in NIH's financial reporting and processes as a material weakness.
- The program has made annual progress on developing treatment strategies that have prolonged and improved the quality of life of HIV-infected individuals. NIH has conducted more than 50 Phase I and Phase II clinical trials of more than 30 vaccine products in human volunteers.
- While progress has been made, based on the current state of science, the AIDS vaccine goal will not be achieved by 2007.

In response to these findings, the Administration will:

1. Adopt the revised goal of extending the timeline for developing an AIDS vaccine from 2007 to 2010, to more realistically reflect the state of the science.
2. Develop targets for the revised goal.

Program Funding Level (in millions of dollars)

2003 Actual	2004 Estimate	2005 Estimate
2,716	2,850	2,930

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research
SUMMARY BY BUDGET MECHANISM

MECHANISM	FY 2003 Actual		FY 2004 Final Conference		FY 2005 Estimate	
Research Grants:	No.	Amount	No.	Amount	No.	Amount
Research Projects						
Noncompeting	2,176	$1,183,933,000	2,243	$1,171,858,000	2,407	$1,268,334,000
Administrative supplements	(129)	20,179,000	(93)	18,204,000	(98)	18,997,000
Full Funded	0	0	0	0	0	0
Single Year	797	290,350,000	1,044	378,368,000	805	307,111,000
Subtotal, competing	797	290,350,000	1,044	378,368,000	805	307,111,000
Subtotal, RPGs	2,973	1,494,462,000	3,287	1,568,430,000	3,212	1,594,442,000
SBIR/STTR	74	23,757,000	91	30,755,000	103	34,686,000
Subtotal, RPGs	3,047	1,518,219,000	3,378	1,599,185,000	3,315	1,629,128,000
Research Centers						
Specialized/comprehensive	62	98,479,000	62	105,851,000	61	111,313,000
Clinical research	0	41,370,000	0	42,712,000	0	44,719,000
Biotechnology	0	6,131,000	2	7,409,000	1	7,632,000
Comparative medicine	17	46,591,000	17	48,112,000	17	51,760,000
Research Centers in Minority Institutions	0	9,510,000	0	9,695,000	0	10,042,000
Subtotal, Centers	79	202,081,000	81	213,779,000	79	225,466,000
Other Research						
Research careers	228	28,340,000	237	30,231,000	239	30,799,000
Cancer education	0	0	0	0	0	0
Cooperative clinical research	25	43,658,000	25	43,708,000	25	44,096,000
Biomedical research support	0	2,197,000	1	2,279,000	1	2,269,000
Minority biomedical research support	2	1,005,000	2	1,032,000	2	1,038,000
Other	108	59,360,000	116	62,977,000	115	63,841,000
Subtotal, Other Research	363	134,560,000	381	140,227,000	382	142,043,000
Total Research Grants	3,489	1,854,860,000	3,840	1,953,191,000	3,776	1,996,637,000
Ruth L. Kirschstein Training Awards:	FTTPs		FTTPs		FTTPs	
Individual awards	52	1,954,000	62	2,691,000	62	2,708,000
Institutional awards	705	29,966,000	717	31,523,000	723	32,217,000
Total, Training	757	31,920,000	779	34,214,000	785	34,925,000
Research & development contracts	178	347,088,000	183	366,241,000	190	400,471,000
(SBIR/STTR)	(2)	(845,000)	(10)	(1,950,000)	(10)	(1,966,000)
Intramural research		318,828,000		326,512,000		330,722,000
Research management and support		93,538,000		96,550,000		98,691,000
Cancer prevention & control		0		0		0
Construction		5,290,000		5,396,000		0
Library of Medicine		7,130,000		7,416,000		7,516,000
Office of the Director		57,564,000		60,432,000		61,435,000
Total, NIH Budget Authority		2,716,218,000		2,849,952,000		2,930,397,000
RoadMap Support		0		9,014,000		11,471,000

NATIONAL INSTITUTES OF HEALTH

Office of AIDS Research

Funding by the NIH Plan for HIV-Related Research
(dollars in thousands)

Research Area	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate	Change
Natural History and Epidemiology	$282,093	$288,893	$290,365	$1,472
Etiology and Pathogenesis	707,563	716,168	726,759	10,591
Therapeutics	731,381	765,349	778,155	12,806
Vaccines	405,063	467,788	514,620	46,832
Behavioral and Social Science	389,519	402,588	406,886	4,298
Training and Infrastructure	158,892	165,655	169,056	3,401
Information Dissemination	41,707	43,511	44,556	1,045
Total, Budget Authority	2,716,218	2,849,952	2,930,397	80,445

National Institutes of Health

Office of AIDS Research

AIDS Funding by Institute and Center

Institute/Center	FY 2003 Actual	FY 2004 Final Conference	FY 2005 Estimate
NCI	$263,285,000	$267,857,000	$268,126,000
NHLBI	74,890,000	75,074,000	75,292,000
NIDCR	25,068,000	25,192,000	25,192,000
NIDDK	29,515,000	30,828,000	31,403,000
NINDS	45,266,000	47,155,000	47,754,000
NIAID	1,309,831,000	1,396,836,000	1,457,464,000
NIGMS	52,044,000	54,570,000	55,073,000
NICHD	125,166,000	130,311,000	134,064,000
NEI	12,694,000	12,663,000	12,663,000
NIEHS	8,533,000	8,717,000	8,772,000
NIA	5,344,000	5,489,000	5,503,000
NIAMS	6,578,000	6,719,000	6,753,000
NIDCD	1,727,000	1,748,000	1,748,000
NIMH	174,851,000	181,219,000	184,111,000
NIDA	301,514,000	312,979,000	315,732,000
NIAAA	25,718,000	26,784,000	27,391,000
NINR	11,800,000	12,083,000	12,336,000
NHGRI	6,698,000	6,877,000	6,917,000
NIBIB	966,000	1,056,000	1,056,000
NCRR	145,965,000	152,544,000	158,126,000
NCCAM	2,700,000	2,800,000	2,800,000
NCMHD	---	---	---
FIC	21,371,000	22,603,000	23,170,000
NLM	7,130,000	7,416,000	7,516,000
OD	57,564,000	60,432,000	61,435,000
B&F	---	---	---
TOTAL, Budget Authority	2,716,218,000	2,849,952,000	2,930,397,000